40. (NEW) The nucleic acid molecule of claim 38, wherein said hybridization conditions are at least as stringent as the following: hybridization in 6X SSC, 1X Denhart solution, 0.1% SDS, 100 mg/mL denatured herring sperm DNA, and at 60 °C overnight; and washing with 0.1X SSC, 0.1% SDS at 65 °C.--

REMARKS

Claims 2-7, 9, and 23-37 were pending in the application. Applicants have amended claims 2, 9, 23-28, 32, and 35-37 and have added new claims 38-40. Applicants have also cancelled claims 6 and 7, without prejudice to or disclaimer of the subject matter contained therein. Applicants reserve the right to pursue the subject matter of the cancelled claims in this or any other patent application. In addition, certain obvious typographical errors in the specification and the claims have been corrected.

No new matter is introduced by these amendments and the amended claims and the new claims are fully supported by the specification as originally filed, as well as specifically as follows: Support for the new claim 38 is found in the specification at, *inter alia*, claim 2(c), and page 9, lines 7-19; support for the new claim 39 is found in the specification at, *inter alia*, page 85, lines 8-11; support for the new claim 40 is found in the specification at, *inter alia*, page 88, lines 3-8; support for the amendment to claim 23 is found in the specification at, *inter alia*, page 10, lines 23-24; support for the amendment to claims 23 and 24, introducing the phrase "isolated, enriched, or purified" is found, *inter alia*, in subsections (d)-(i) of original claim 2, which in turn was dependent on original claim 1, which recited the phrase in its preamble; support for the amendment to claims 9 and 28 is found, *inter alia*, in the fact that they are dependent on claims 2, 23, or 24, and include all of their limitations; support for the amendment to claim 36 is found in the specification at, *inter alia*, page 95, lines 21-22; support for the amended claim 37 is found, *inter alia*, in the definition of a nucleic acid molecule, in the specification at page 7, line 23, to page 8, line 2, and in Example 4, at page 93, line 4, to page 100, line 19.

Applicants attach hereto as Appendix A the text of the claims as they are pending following the present amendments.

Applicants respond below to the Examiner's rejections and objections as set forth in the Office Action.

I. Rejections Based on 35 U.S.C. § 112, Second Paragraph

Claims 2-7, 9, and 23-37 stand rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite.

A. "ALK-7 Polypeptide"

Claims 2, 9, 23-25, and 35 stand rejected for allegedly being vague and indefinite in the recitation of "ALK-7 polypeptide." Without acquiescing to the Examiner's arguments, Applicants have amended the claims and have removed the phrase therefrom. Reference in the claims is now made to the amino acid sequence set forth in SEQ ID NO:2. Therefore, Applicants request that the Examiner reconsider and withdraw the rejection.

B. Complementary Nucleic Acids

Claims 2, 23, and 24 stand rejected for allegedly being vague and indefinite in the recitation "complement" of a nucleic acid molecule. The Examiner has suggested that replacing "complement" with "completely complementary" would obviate the rejection. Applicants have amended the claims as suggested by the Examiner. In view of the above, Applicants request that the Examiner reconsider and withdraw the rejection.

C. Highly Stringent Conditions

Claim 2 stands rejected for allegedly being vague and indefinite in the recitation "highly stringent conditions." Applicants have amended the claim and have removed subsection (c) of the claim. Applicants have re-introduced the subject matter of subsection (c) of claim 2 as new claim 38. Also, in new claim 38, specific conditions for the lower limit of stringency are recited. Thus, Applicants request that the Examiner reconsider and withdraw the rejection.

D. Claim 23(c)

Subsection (c) of claim 23 stands rejected for allegedly being vague and indefinite. Applicants submit that the recitation of "193-489" and "or SEQ ID NO:2" in the claim were typographical errors. Claim 23 comprises the subject matter of subsections (d)-(g) of original claim 2, wherein in said subsection (d) the amino acid segments set forth in the presently amended claims are recited. Applicants have amended the claim to recite the correct amino acid segments of SEQ ID NO:2. The amended subsection (c) is drawn toward a nucleic acid molecule encoding the fragments of a polypeptide having the amino acid sequence set forth in SEQ ID NO:2. The subsection is not drawn toward a nucleic acid molecule encoding the polypeptide having the amino acid sequence set forth in SEQ ID NO:2 in its entirety.

In view of the above, Applicants request that the Examiner reconsider and withdraw the rejection.

E. Recitation of "Having"

Claims 2, 23, 24, 35, and 37 stand rejected for allegedly being vague and indefinite in the recitation "having." Applicants have amended the claims and have replaced the word "having" with the word "comprising."

In view of the above, Applicants request that the Examiner reconsider and withdraw the rejection.

F. Claims 6 and 7

Claims 6 and 7 stand rejected for allegedly being vague and indefinite. Claim 7 stands rejected for allegedly lacking proper antecedent basis. Since Applicants have cancelled these claims, the rejection is now moot. Therefore, Applicants request that the Examiner withdraw the rejection.

G. Recitation of "Having"

Claim 27 stands rejected for allegedly being vague and indefinite in the recitation "corresponding." Applicants have amended the claim and have replaced the word "corresponding" with the word "comprising."

In view of the above, Applicants request that the Examiner reconsider and withdraw the rejection.

H. Claims 36 and 37

Claims 36 and 37 stand rejected for allegedly being vague and indefinite in the recitation "ALK-7DN" and "ALK-7TD," respectively. Applicants have amended the claims and have incorporated the definition of ALK-7DN, found in the specification at page 95, lines 21-22, into claim 36. Furthermore, Applicants have removed the recitation of "ALK-7TD" from claim 37.

In view of the above, Applicants request that the Examiner reconsider and withdraw the rejection.

II. Rejections Based on 35 U.S.C. § 112, First Paragraph

Claim 23 is rejected under 35 U.S.C. § 112, first paragraph, for allegedly introducing new matter into the specification by reciting a segment of the amino acid sequence of SEQ ID NO:2. As Applicants discussed above, in part I(D) of the present response, the fragment was introduced into the claim because of a typographical error. Applicants have amended the claim and have corrected this error. Support for this amendment is given above.

In view of the above, Applicants request that the Examiner reconsider and withdraw the rejection.

III. Rejections Based on 35 U.S.C. § 101

Claims 9, 23, 24, 28, and 37 are rejected under 35 U.S.C. § 101 for allegedly not being drawn to a statutory subject matter. The Examiner alleges that the claims are "directed to nucleic acid molecules without a recitation indicating the hand of man."

Applicants have amended the claims and have included the phrase "isolated, enriched, or purified" into the preamble of each claim. Support for these amendments is found as follows. Claims 23 and 24 are directed to the subject matter of subsections (d)-(i) of original claim 2, which in turn was dependent on original claim 1, which recited the phrase in its preamble. Claims 9 and 28 are dependent on claims 2, 23, or 24, and include

all of their limitations. Support for the amended claim 37 is found, *inter alia*, in the definition of a nucleic acid molecule, in the specification at page 7, line 23, to page 8, line 2, and in Example 4, at page 93, line 4, to page 100, line 19.

IV. Rejections Based on 35 U.S.C. § 102

A. Rejections Based on 35 U.S.C. § 102(e) Over the Ibañez Patents

Claims 2-7, 9, and 27-33 stand rejected under 35 U.S.C. § 102(e) for allegedly being anticipated by Ibañez '609,[1] Ibañez '565,[2] or Ibañez '245[3] (collectively "the Ibañez Patents"). All three patents disclose the same amino acid and nucleic acid sequences. The Examiner alleges that the Ibañez Patents disclose "a nucleic acid molecule which is the same as that of Claims 2 and 27."

Applicants respectfully traverse. The Ibañez Patents do not disclose the same amino acid sequence as that set forth in SEQ ID NO:2 of the present application. The amino acid sequence disclosed by the Ibañez Patents differs from the amino acid sequence of the present application by 32 amino acids. That is, the two sequences are only 93% homologous. Furthermore, the two sequences differ in all the fragments claimed in claim 23(c). For example, there are 11 differences in amino acid residues 1-25; 2 differences in amino acid residues 26-113; 19 differences in amino acid residues 114-493; 15 differences in amino acid residues 137-493; and 8 differences in amino acid residues 193-489.

Furthermore, the Examiner states that the Ibañez Patents disclose "a nucleic acid molecule which would hybridize to the complement of a nucleotide sequence which encodes a polypeptide comprising the full length amino acid sequence of SEQ ID NO:2." Applicants respectfully traverse this rejection as well. The specification, at page 8, line 21, to page 9, line 6, states that the hybridization conditions of the invention are such that they would "prevent hybridization of nucleic acids having one or two mismatches out of 20 contiguous nucleotides." As mentioned above, the Ibañez Patents disclose a nucleic acid molecule which encodes an amino acid sequence that is different from the amino

[1] Ibañez et al., U.S. Patent No. 6,614,609.
[2] Ibañez et al., U.S. Patent No. 5,789,565.
[3] Ibañez et al., U.S. Patent No. 5,811,245.

acid sequence of SEQ ID NO:2 by 32 out of 493 amino acids. This means that the nucleic acid molecule of the Ibañez Patents is different from the nucleic acid molecule of the invention, by at least 96 out of 1479 bases, which is 1 out of 15.5 mismatches. This number is far greater than the upper limit that the specification puts on the acceptable rate of mismatches. Therefore, the claims of the invention do not read on the nucleic acid molecule of the Ibañez Patents.

Since the amino acid sequences are different, the Ibañez Patents do not disclose all the limitations of the claims of the present invention. Therefore, the Ibañez Patents do not anticipate the present claims.[4] In view of the above, Applicants respectfully request that the Examiner reconsider and withdraw the rejection.

B. Rejections Based on 35 U.S.C. § 102(a) Over Ryden et al.

Claims 2, 3, 5-7, 9, 23, 24, and 32 are rejected under 35 U.S.C. § 102(a) for allegedly being anticipated by Ryden et al.[5] The Examiner alleges that "Ryden et al. disclose the deduced amino acid sequence of ALK-7 . . . ."

Applicants respectfully submit that to the extent this rejection is directed towards the cancelled claims 6 and 7 the rejection is moot. As for the rejection of the other claims, Applicants respectfully traverse. Ryden et al.do not disclose the same amino acid sequence as that set forth in SEQ ID NO:2 of the present application. The amino acid sequence disclosed by Ryden et al. differs from the amino acid sequence of the present application by 35 amino acids. That is, the two sequences are less than 93% homologous. Furthermore, the two sequences differ in all the fragments claimed in claim 23(c). For example, there are 17 differences in amino acid residues 1-25; 3 differences in amino acid residues 26-113; 21 differences in amino acid residues 114-493; 16 differences in amino acid residues 137-493; and 8 differences in amino acid residues 193-489.

Since the amino acid sequences are different, Ryden et al. do not disclose all the limitations of the claims of the present invention. Therefore, Ryden et al. do not

[4] *See*, for example, *Verdegaal Bros. v. Union Oil Co. of California*, 2 USPQ2d 1051 (Fed. Cir. 1987) holding that "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *See*, also M.P.E.P. § 2131.
[5] Ryden et al. *J. Biol. Chem.*, 271:48, 30603-30609 (1996).

anticipate the present claims. In view of the above, Applicants respectfully request that the Examiner reconsider and withdraw the rejection.

V. Rejections Based on 35 U.S.C. § 103(a)

Claim 34 stands rejected based on 35 U.S.C. § 103(a) for allegedly being unpatentable over the Ibañez Patents individually in view of Hammonds et al.[6] The Examiner states that the Ibañez Patents disclose the nucleic acid molecule of claim 2 and that Hammonds et al. disclose cloning a nucleic acid molecule using a pRK5 expression plasmid.

Applicants respectfully traverse. As discussed above, the Ibañez Patents do not disclose the amino acid sequence set forth in SEQ ID NO:2 and therefore do not disclose the nucleic acid molecule of claim 2. Thus, there is no teaching or motivation in the cited documents to combine the nucleic acid molecule of claim 2 with the pRK5 expression plasmid in order to reach the invention claimed in claim 34.[7] The Examiner, therefore, has not met his burden of establishing a *prima facie* case of obviousness.

In view of the above, Applicants respectfully request that the Examiner reconsider and withdraw the rejection.

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[6] Hammonds et al., U.S. Patent No. 5,168,050.

[7] "Obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the reference s themselves or in the knowledge generally available to one of ordinary skill in the art." M.P.E.P. § 2143.01, *citing In re Fine*, 5 USPQ2d 1596 (Fed. Cir. 1988), and *In re Jones*, 21 USPQ2d 1941 9 Fed. Cir. 1992).

CONCLUSION

In view of the above, Applicants respectfully submit that the claims are in condition of allowance. Applicants respectfully request that the Application be allowed and passed to issue. Applicants have enclosed a petition for a one month extension of time and a check for $110.00. If this amount is incorrect, please charge or credit Lyon & Lyon Deposit Account No. 12-2475 for the appropriate amount. Should the Examiner believe that a telephone interview would aid in the prosecution of this application, Applicants encourage the Examiner to call the undersigned collect at (858) 552-8400.

Respectfully submitted,

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APPENDIX A
CURRENTLY PENDING CLAIMS

2. An isolated, enriched or purified nucleic acid molecule which comprises a nucleotide sequence that

(a) encodes a polypeptide comprising the full length amino acid sequence set forth in SEQ ID NO:2; or

(b) is completely complementary to the nucleotide sequence of (a).

3. The nucleic acid molecule of claim 2, wherein said nucleic acid molecule is isolated, enriched, or purified from a mammal.

4. The nucleic acid molecule of claim 3, wherein said mammal is a human.

5. The nucleic acid molecule of claim 2, further comprising a vector or promoter effective to initiate transcription in a host cell.

9. A recombinant cell comprising an isolated, enriched or purified nucleic acid molecule encoding either the polypeptide according to Claim 2, Claim 23 or Claim 24 or the polypeptide according to Claim 2, Claim 23 or Claim 24 fused to a second polypeptide.

23. An isolated, enriched, or purified nucleic acid molecule comprising a nucleotide sequence that

(a) encodes a polypeptide comprising the full length amino acid sequence of the sequence set forth in SEQ ID NO:2, except that it lacks one or more, but not all, of the following segments of amino acid residues of SEQ ID NO: 2: 1-25, 26-113, 114-493, 137-493 or 193-483;

(b) is completely complementary to the nucleotide sequence of (a);

(c) encodes a polypeptide comprising the amino acid sequence set forth in SEQ ID NO: 2 from at least one but not all of amino acid residues 1-25, 26-113, 114-493, 137-493 or 193-483 of SEQ ID NO:2; or

(d) is the complement of the nucleotide sequence of (c).

24. An isolated, enriched, or purified nucleic acid molecule comprising a nucleotide sequence that

(a) encodes a polypeptide comprising the full length amino acid sequence set forth in SEQ ID NO:2, except that it lacks one or more, but not all, of the domains selected from the group consisting of a signal peptide domain, an extracellular region, a transmembrane domain, a cytoplasmic domain and a catalytic domain; or

(b) is completely complementary to the nucleotide sequence of (a).

25. The nucleic acid molecule of Claim 2, Claim 23 or Claim 24, further comprising a nucleotide sequence that encodes a second polypeptide, wherein said second polypeptide is fused to said polypeptide.

26. The nucleic acid molecule of Claim 2, Claim 23 or Claim 24, wherein said nucleic acid molecule further encodes a GST-fusion protein.

27. An isolated, enriched or purified nucleic acid molecule comprising the nucleotide sequence set forth in SEQ ID NO:1.

28. The isolated, enriched, or purified nucleic acid molecule of Claim 2, Claim 23 or Claim 24, further comprising restriction endonuclease recognition sites at the 5'end and/or 3'end,

so that the nucleic acid molecule is manipulable to contain functional alterations of the nucleic acid sequence that afford an opportunity to promote secretion and/or processing of heterologous proteins encoded therefrom.

29. The nucleic acid molecule of Claim 5, wherein said vector is selected from the group consisting of pBR322, pUC118, pUC119, ColE1, pSC101, pACYC 184, pVX, pC194, pC221, pT127, p1J101, BPV, vaccinia, SV40, 2-micron circle, λgt10, λgt11, fC31, pMAM-neo and pKRC.

30. The nucleic acid molecule of Claim 5, wherein said promoter is selected from the group consisting of the int promoter of bacteriophage λ, the bla promoter of the β-lactamase gene sequence of pBR322, the CAT promoter of the chloramphenicol acetyl transferase gene sequence of pBR325, the major right or left promoters of bacteriophage λ, the trp, recA, lacZ, lacI or gal promoters of E. coli and the α-amylase or sigma-28 specific promoters of B. subtilis.

31. The nucleic acid molecule of Claim 5, wherein said host cell is a yeast cell, a fungi cell, an insect cell, a plant cell or a mammalian cell, said mammalian cell either in vivo or in tissue culture.

32. The nucleic acid molecule of Claim 31, wherein said mammalian cell is selected from the group consisting of a COS Cell, an HEK293 cell, a VERO cell, a 3T3 cell, a CHO-K1 cell, a 32D cell, an SP2/0 cell, a J558L cell, an IMR 332 cell and a PC12 cell.

33. The nucleic acid molecule of Claim 5,wherein said host cell is eukaryotic, and wherein said promoter is selected from the group consisting of a mouse metallothionein I promoter, the TK promoter of Herpes virus, the SV40 early promoter and the yeast ga14 promoter.

34. The nucleic acid molecule of Claim 5, wherein said vector is pAdRSVOES or pRK5.

35. An isolated, enriched or purified nucleic acid molecule comprising a nucleotide sequence that encodes a polypeptide comprising the full length amino acid sequence set forth in SEQ ID NO:2, except that said polypeptide is truncated and signaling incompetent and/or dominant negative.

36. The nucleic acid molecule of Claim 35, wherein said truncated polypeptide is obtained by insertion of an HA-tag at position 230 of the amino acid sequence set forth in SEQ ID NO:2.

37. An isolated, enriched, or purified nucleic acid molecule encoding a constitutively active polypeptide, wherein said nucleic acid molecule comprises a nucleotide sequence that encodes a polypeptide comprising the full length amino acid sequence set forth in SEQ ID NO:2, except that said amino acid sequence contains an Asp at position 194 of SEQ ID NO:2 instead of a Thr.

38. An isolated, enriched or purified nucleic acid molecule which encodes a naturally occurring polypeptide and hybridizes to the nucleic acid molecule of claim 2 under hybridization conditions at least as stringent as the following: hybridization in 50% formamide, 5X SSC, 50 mM NaH_3PO_4, pH 6.8, 0.5% SDS, 0.1 mg/mL sonicated salmon sperm DNA, and 5X Denhart solution at 42 °C overnight; and washing with 0.2X SSC, 0.1% SDS at 45 °C at least twice, wherein the nucleic acid molecule of claim 2 comprises the nucleotide sequence that is completely complimentary to the nucleotide sequence that encodes the polypeptide comprising the full length sequence set forth on SEQ ID NO:2.

39. The nucleic acid molecule of claim 38, wherein said hybridization conditions are at least as stringent as the following: hybridization in 6X SSC, 1X Denhart solution, 0.1% SDS, 0.1 mg/mL denatured, fragmented salmon sperm DNA, and at 65 °C overnight; and washing with 0.1X SSC, 0.1% SDS at 65 °C.

40. The nucleic acid molecule of claim 38, wherein said hybridization conditions are at least as stringent as the following: hybridization in 6X SSC, 1X Denhart solution, 0.1% SDS, 100 mg/mL denatured herring sperm DNA, and at 60 °C overnight; and washing with 0.1X SSC, 0.1% SDS at 65 °C.